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The Constituents of *Schizandra chinensis* BAILL. The Structures of Two New Lignans, Pre-gomisin and Gomisin J

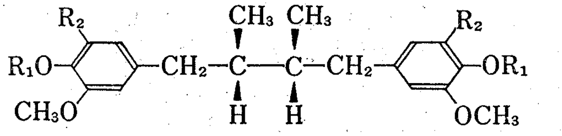
Two new lignans, pre-gomisin(I) and gomisin J(II) have been isolated from the fruits of *Schizandra chinensis* BAILL. (Schizandraceae). Their structures were established by chemical and spectral evidence.

Keywords——*Schizandra chinensis* BAILL.; Schizandraceae; lignan; pre-gomisin; gomisin J; desoxyschizandrin; NOE; CD spectrum

In the previous papers of this series, it was reported that the petroleum ether extract of the fruits of *Schizandra chinensis* BAILL. (Schizandraceae) contains nine new dibenzocyclooctadiene lignans.[1] This paper is concerned with isolation and characterization of two additional new lignans named pre-gomisin(I, yield 0.012%) and gomisin J(II, 0.023%) isolated from the same source.

Pre-gomisin(I): $C_{22}H_{30}O_6$(M^+, *m/e*, 390),[2] colourless prisms, mp 130—131.5°, $[\alpha]_D^{25}$ 0°(c=0.44).[3] Ultraviolet (UV) spectrum λ_{max}^{EtOH} nm (log ε): 208(4.81), 225(sh 4.30), 270(3.15). Infrared (IR) spectrum ν_{max}^{KBr} cm^{-1}: 3370(OH), 1608, 1588(aromatic). Proton nuclear magnetic resonance (PMR) spectrum (δ in $CDCl_3$): 0.85 (6H, d, J=6 Hz, 2×C$\underline{H}_3$-$\overset{|}{\underset{|}{C}}$H), 1.77 (2H, m, 2×-$\overset{|}{\underset{|}{C}}$H), 1.90—2.87 (4H, m, 2×Ar-C$\underline{H}_2$-), 3.83 (6H, s, 2×OCH_3), 3.87 (6H, s, 2×OCH_3), 5.87 (2H, s, 2×OH, disappeared on addition of D_2O), 6.28 (2H, d, J=2 Hz, 2×arom.-H), 6.43 (2H, d, J=2 Hz, 2×arom.-H). $FeCl_3$: green, Gibbs test: blue.

The UV spectrum of I resembles those of *meso*-dihydroguaiaretic acid[4] and *seco*-isolaricirenol,[5] suggesting that I should be a 2,3-dimethyl-1,4-diphenylbutane type lignan.



I	$R_1=CH_3$	$R_2=OH$	IIIa	$R_1=H$	$R_2=NO_2$
Ia	$R_1=CH_3$	$R_2=OCOCH_3$	IIIb	$R_1=CH_3$	$R_2=NO_2$
III	$R_1=H$	$R_2=H$	IIIc	$R_1=CH_3$	$R_2=NH_2$

$$\text{III} \xrightarrow[\text{yield, 28.5\%}]{\substack{\text{1\% HNO}_3\text{, 0°} \\ \text{AcOH/AcOEt}}} \text{IIIa} \xrightarrow[\text{95.5\%}]{\substack{(\text{CH}_3)_2\text{SO}_4 \\ \text{K}_2\text{CO}_3\text{, acetone}}} \text{IIIb} \xrightarrow[\text{76.3\%}]{\substack{\text{Sn/HCl} \\ \text{65°, 1 hr}}} \text{IIIc} \xrightarrow[\text{2) 5\% H}_2\text{SO}_4\text{, 38\%}]{\substack{\text{1) NaNO}_2\text{/DMSO} \\ \text{c-H}_2\text{SO}_4\text{-H}_2\text{O}}} \text{I}$$

Chart 1

On acetylation (Ac_2O/pyridine), I gave a diacetate (Ia), $C_{26}H_{34}O_8$,[2] colourless prisms, mp 124—125°, $[\alpha]_D^{25}$ 0° (c=0.65)[3], UV λ_{max}^{EtOH} nm (log ε): 205 (4.79), 223 (sh 4.22), 274 (3.45): IR ν_{max}^{KBr} cm^{-1}: 1758 (>C=O), 1603, 1580 (aromatic): PMR (δ in $CDCl_3$): 0.85 (6H, d, J=6 Hz, 2×C$\underline{H}_3$-$\overset{|}{\underset{|}{C}}$H), 1.70 (2H, m, 2×-$\overset{|}{\underset{|}{C}}$H), 2.30 (6H, s, 2×OAc), 2.08—3.00 (4H, m, 2×Ar-C$\underline{H}_2$-), 3.80

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1) *a*) H. Taguchi and Y. Ikeya, *Chem. Pharm. Bull.* (Tokyo), **23**, 3296 (1975); *b*) H. Taguchi and Y. Ikeya, *ibid.*, **25**, 364 (1977); *c*) Y. Ikeya, H. Taguchi, and Y. Iitaka, *Tetrahedron Lett.*, **1976**, 1359; *d*) Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **26**, 328 (1978).

2) Elemental analysis of the compounds gave satisfactory results.

3) All specific rotations were measured as chloroform solutions.

4) A.W. Schrecker, *J. Am. Chem. Soc.*, **79**, 3823 (1957); F.E. King and J.G. Wilson, *J. Chem. Soc.*, **1964**, 4011; C.W. Perry, *C. A.*, **73**, 45118*t* (1970).

5) L.H. Briggs, R.C. Cambie, and J.L. Hoare, *Tetrahedron*, **7**, 262 (1959).

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(6H, s, 2×$\mathrm{OCH_3}$), 3.83 (6H, s, 2×$\mathrm{OCH_3}$), 6.47 (2H, d, J=2 Hz, 2×arom.–H), 6.57 (2H, d, J=2 Hz, 2×arom.–H). On the basis of the above spectral data and the result of Gibbs test, I was suggested to be 1,4-bis(3-hydroxy-4,5-dimethoxyphenyl)-2,3-dimethylbutane. In order to confirm the structure, I was thus prepared from *meso*-dihydroguaiaretic acid (III) by the procedure shown in Chart 1.[4,6] The product (I), $\mathrm{C_{22}H_{30}O_6}$, mp 129—131°, was identified with pre-gomisin by the direct comparison (IR, mixed mp, PMR and TLC). On the other hand, the circular dichroism (CD) spectrum of pre-gomisin (I) shows no Cotton effect in the region 300—200 nm, indicating that I possesses 2-*R* and 3-*S* configurations (*meso*-form). Consequently, the structure of pre-gomisin is now characterized to be (2*R*, 3*S*)-1,4-bis(3-hydroxy-4,5-dimethoxyphenyl)-2,3-dimethylbutane.

Gomisin J (II): $\mathrm{C_{22}H_{28}O_6}$ ($\mathrm{M^+}$, *m/e*, 388),[2] mp 149—150°, $[\alpha]_D^{24}$ −43.9° (c=1.00),[3] UV λ_{max}^{EtOH} nm (log ε): 214 (4.70), 248 (4.15), 276 (3.53); IR ν_{max}^{KBr} $\mathrm{cm^{-1}}$: 3545, 3450 (OH), 1610, 1583 (aromatic); PMR (δ in $\mathrm{CDCl_3}$): 0.75 (3H, d, J=7 Hz, $\mathrm{C_{(8)}}$–$\mathrm{CH_3}$), 0.99(3H, d, J=7 Hz, $\mathrm{C_{(7)}}$–$\mathrm{CH_3}$), 1.5—2.4(2H, m, $-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 2.0—2.7 (4H, m, Ar–$\mathrm{C\underline{H}_2}$–), 3.50 (6H, s, $\mathrm{C_{(1)\,(14)}}$–$\mathrm{OCH_3}$, shielded by the aromatic rings[7]), 3.94 (6H, s, 2×$\mathrm{OCH_3}$), 5.91 (2H, s, 2×OH, disappeared on addition of $\mathrm{D_2O}$), 6.63(2H, s, 2×arom.–H). $\mathrm{FeCl_3}$ in pyridine–chloroform: green.

The above spectral data suggested that gomisin J is a dibenzocyclo-octadiene lignan, having four methoxyl and two hydroxyl groups on the aromatic rings.[1] Furthermore, the PMR spectrum of II shows two distinct methyl signals, suggesting that one methyl group (δ 0.75) is shielded by the aromatic ring and II has, therefore, a *cis*-dimethyl configuration.[8b] Methylation of II ($\mathrm{Me_2SO_4/K_2CO_3}$ in acetone, reflux) afforded IV, colourless prisms, $\mathrm{C_{24}H_{32}O_6}$,[2] mp 113.5—115° (*n*-hexane–ether), $[\alpha]_D^{26}$ −65.7° (c=1.37),[3] which was identified with desoxyschizandrin (*dl*-form, CD: $[\theta]_{300-200}$ 0° (MeOH), mp 109.5—110.5°)[8] isolated from the same source (IR, PMR and TLC). In order to confirm the position of two hydroxyl groups in II, the intramolecular nuclear Overhauser effects (NOE) in II and its dibenzyl ether (IIa) ($\mathrm{C_6H_5CH_2Cl/K_2CO_3}$ in acetone, reflux) were measured (in $\mathrm{CDCl_3}$)[1] (Chart 2). Irradiation of the methoxyl signals in II showed no enhancement in the integrated intensity of the aromatic protons, however, in IIa, irradiation of the benzylic methylene signals (δ 5.12(s), 5.15(s)) showed enhancement of the integrated intensities of the both aromatic protons, indicating that two hydroxyl groups are located at the vicinal positions of the aromatic protons. On the basis of the above results and the CD spectrum of IV ($[\theta]^{25}$(nm): −9800 (sh 278), −83000 (248), −62000 (236), +62000 (214) (c=0.0077, MeOH), biphenyl *S*-configuration[1b]), the absolute structure of gomisin J is thus elucidated as II.

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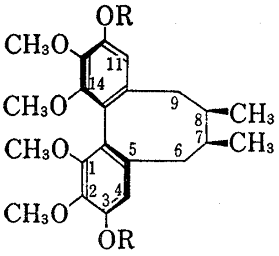
6) The compound (III) was derived from guaiaretic acid by catalytic hydrogenation (Pd-C, MeOH) and its structure was confirmed as dimethyl ether.[4] Dimethyl ether of III: $\mathrm{C_{22}H_{34}O_4}$,[2] colourless needles, mp 99.5—100.5°, (lit. 101—102°), UV λ_{max}^{EtOH} nm(log ε): 229(4.26), 280(3.80), 285(sh 3.72); PMR(δ in $\mathrm{CCl_4}$): 0.82(6H, d, J=6 Hz, $\mathrm{C\underline{H}_3}$–$\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 1.72(2H, m, $-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 2.02—2.82(4H, m, Ar–$\mathrm{C\underline{H}_2}$–), 3.73(12H, s, 4×$\mathrm{OCH_3}$), 6.38(6H, m, arom.–H). IIIa: $\mathrm{C_{20}H_{24}N_2O_8}$,[2] mp 173—174.5°, orange prisms(acetone), $[\alpha]_D^{23}$ 0°(c=0.3),[3] UV λ_{max}^{EtOH} nm (log ε): 225(4.32), 254(sh 3.87), 296(3.90); IR ν_{max}^{KBr} $\mathrm{cm^{-1}}$: 3200(OH), 1615(aromatic), 1540, 1325($\mathrm{NO_2}$): PMR(δ in d_6-acetone): 0.88(6H, d, J=7 Hz, $\mathrm{C\underline{H}_3}$–$\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 1.85(2H, m, $-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 2.22—3.00(4H, m, Ar–$\mathrm{C\underline{H}_2}$–), 3.83(3H, s, $\mathrm{OCH_3}$), 3.88(3H, s, $\mathrm{OCH_3}$), 7.05, 7.15, 7.32, 7.42(each 1H, d, J=2 Hz(*meta* coupling), 4×arom.–H). IIIb: $\mathrm{C_{22}H_{28}N_2O_8}$,[2] mp 107.5—110°, $[\alpha]_D^{21}$ 0°(c=1.11),[3] UV λ_{max}^{EtOH} nm(log ε): 222(4.43), 265(3.66), 330(3.23); IR ν_{max}^{KBr} $\mathrm{cm^{-1}}$: 1610(aromatic), 1540, 1350($\mathrm{NO_2}$); PMR(δ in $\mathrm{CCl_4}$): 0.85 (6H, d, J=6 Hz, $\mathrm{C\underline{H}_3}$–$\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 1.75(2H, m, $-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H}$), 2.05—2.95(4H, m, Ar–$\mathrm{C\underline{H}_2}$–), 3.82(3H, s, $\mathrm{OCH_3}$), 3.88 (9H, s, 3×$\mathrm{OCH_3}$), 6.73, 6.80, 6.90, 6.97(each 1H, d, J=2 Hz, 4×arom.–H).

7) A.F.A. Wallis, *Tetrahedron Lett.*, **1968**, 5287.

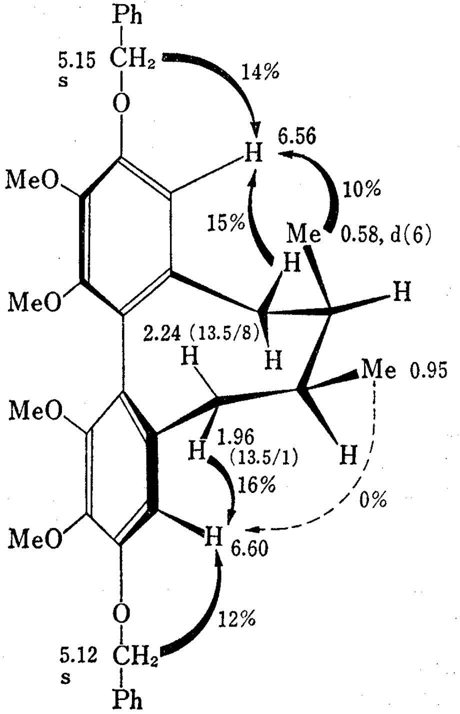
8) *a*) N.K. Kochetkov, A. Khorlin, and O.S. Chizov, *Tetrahedron Lett.*, **1962**, 361; *b*) E. Ghera, Y. Ben-David and D. Becker, *ibid.*, **1977**, 463; *c*) The conformation of cyclo-octadiene ring in desoxyschizandrin is suggested to be the same twist-boat-chair form[9] as the other lignans isolated from this plant on the basis of PMR, CMR specral and chemical studies (the data would be published in the continued report). *d*) *d*-desoxyschizandrin (mp 113.5—115°, colourless prisms(*n*-hexane–ether), $[\alpha]_D^{23}$ +92.1°(c=2.73)[3]), has been isolated from the another source collected in the market.

9) F.A.L. Anet and I. Yavari, *Tetrahedron Lett.*, **1975**, 1567.

The occurrence of I and II in this plant is interesting, since they are assumed to be the precursors in the possible biogenetical route of the oxygenated dibenzocyclo-octadiene lignans such as gomisin A–D, F and G[1] as shown in Chart 3.



II : R=H
IV : R=CH_3



NOE in IIa [δ in $CDCl_3$ (J=Hz)]
Chart 2

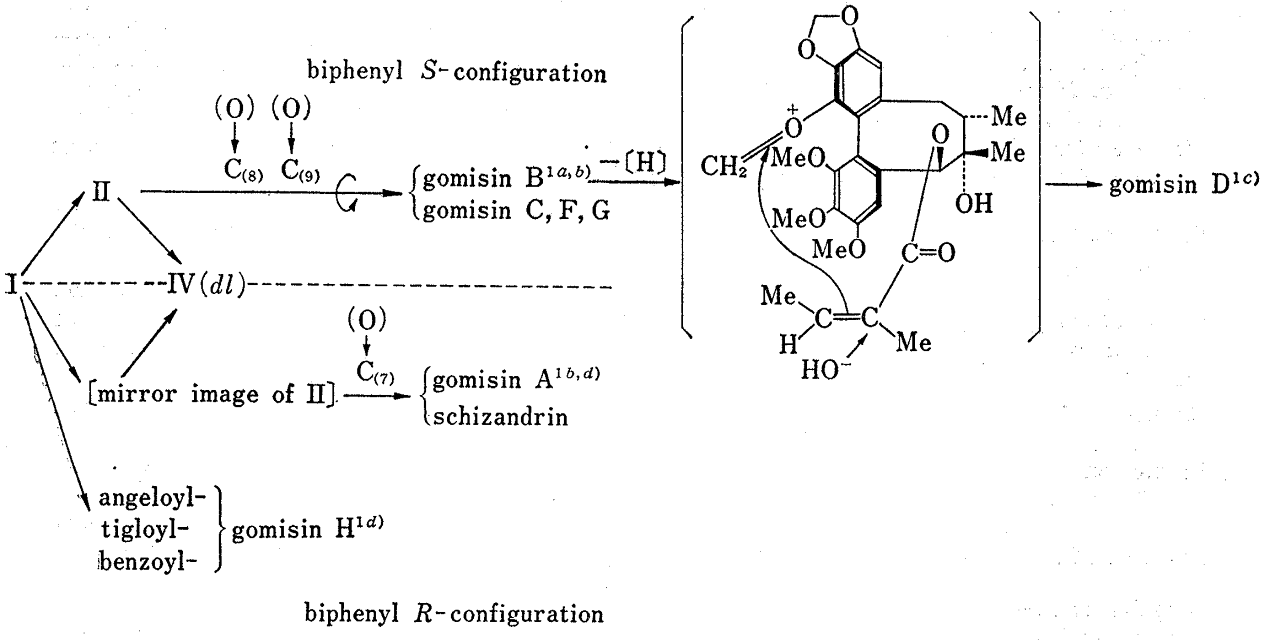


Chart 3. Possible Biogenetical Route of Gomisins

Tsumura Laboratory
1421, Izumi, Komae-shi,
Tokyo

Yukinobu Ikeya
Heihachiro Taguchi
Itiro Yosioka

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